

The section header 'In vitro Pyrogen Test' is written in a bold, blue, sans-serif font. It is located in the upper left quadrant of the page, partially overlapping a white circular graphic element. Below the header is a thin blue horizontal line.

Exposure of the human body to pyrogenic compounds causes fever and inflammation. In the case of medical devices such adverse reactions can be induced by surface contamination as well as by the physical-chemical properties of the material surface in itself. This is particularly true for surfaces coated with polymers, bio-molecules and drugs. Therefore regulatory requirements demand that all implantable medical devices are tested for their potential pyrogenicity.

### **Pyrogen test: a new validated in vitro method**

The **in vitro pyrogen test** is an internationally validated method which measures the release of cytokines from human blood cells exposed to pyrogenic compounds or material surfaces in vitro.

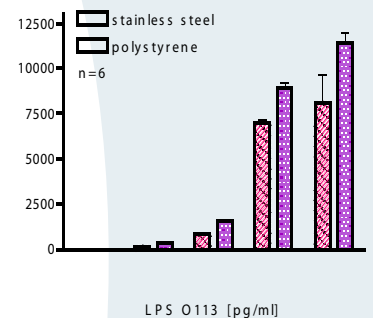
#### **Advantages of the in vitro pyrogen test:**

- Detection of a wide range of pyrogens (endotoxins and non-endotoxins)
- Use of human blood in vitro is more relevant to the physiological in vivo situation
- Replacement of the in vivo rabbit pyrogen test
- The test is internationally validated

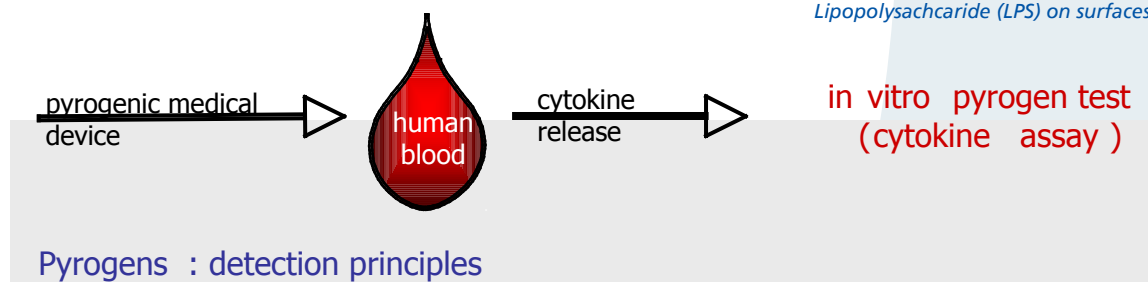
# In vitro Pyrogen Test

## Blood/device interaction

Implants are coming in direct contact with the patient (blood/device interaction) can cause health problems. According to the existing guidelines, all these devices have to be sterilized and decontaminated, to prevent any kind of infection or inflammation. But an artificial surface may also interact itself with the organism e.g. via the mammalian blood stream.



Endotoxin:  
Lipopolysachcaride (LPS) on surfaces



### Step 1:

Collection of heparinised blood from healthy donors

### Step 2:

Incubation with medical device

### Step 3:

Analyse cytokine concentration in blood by immunoassay (Interleukin-1 $\beta$ : IL-1 $\beta$ )

### References:

Fennrich S, Fischer M, Hartung T, Lexa P, Montag-Lessing T, Sonntag HG, Weigandt M, Endel A. Detection of endotoxins and other pyrogens using human whole blood. *Dev Biol Stand* 1999;101:131-139  
Fennrich S, Wendel A, Hartung T. New applications of the human whole blood assay (PyroCheck). *Altex* 1999;16:146-9  
Mazotti F, Hartung T, von Aulock S. In vitro pyrogen test-a new method for solid medical devices. *J Biomed Mater Res A* 2007;80:276-282

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